REMARKS

The December 31, 2009 Official Action and the references cited therein have been carefully reviewed. In view of the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset, a shortened statutory response period of three (3) months was set forth in the December 31, 2009 Official Action. Therefore, the initial due date for response is March 31, 2010.

The Examiner has rejected claims 38, 39, 41-47, and 54-56 under 35 U.S.C. §103(a) as allegedly unpatentable over U.S Patent Application Publication No. 2001/0001040 in view of U.S Patent 5,902,610.

Claims 38, 39, 43-47, 55 and 56 have also been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 35 and 36 of copending U.S. Patent Application No. 10/550,444 in view of the '040 application and the '610 patent. Applicants continue to respectfully disagree with the Examiner's position for the reasons of record. However, in the sole interest of expediting prosecution of the instant application, Applicants submit herewith a Terminal Disclaimer, thereby overcoming the instant rejection. Withdrawal of the double patenting rejection is respectfully requested.

The foregoing rejections constitute all of the grounds set forth in the December 31, 2009 Official Action for refusing the present application.

No new matter has been introduced into this application by reason of any of the amendments presented herewith.

In view of the reasons set forth in this response, Applicants respectfully submit that the 35 U.S.C. §103(a) rejection of claims 38, 39, 41-47, and 54-56 and the double patenting rejection of claims 38, 39, 43-47, 55 and 56, as set forth in the December 31, 2009 Official Action, cannot be maintained. These grounds of rejection are, therefore, respectfully traversed.

CLAIMS 38, 39, 41-47, AND 54-56 ARE NOT RENDERED OBVIOUS BY THE '040 APPLICATION IN VIEW OF THE '610 PATENT

The Examiner has rejected claims 38, 39, 41-47, and 54-56 under 35 U.S.C. §103(a) as allegedly unpatentable over the '040 application in view of the '610 patent. The '040 application allegedly discloses that IDO inhibitors including 1-MT are useful in the treatment of cancer. The '610 patent allegedly teaches that cisplatin is an anticancer that is effectively used against a broad spectrum of cancers. It is the Examiner's position that it would have been obvious to a skilled artisan to combine the above disclosures to arrive at the instantly claimed invention.

At pages 5 and 6 of the instant Official Action, the Examiner acknowledges that the instant application demonstrates a greater than additive effect with the administration of an IDO inhibitor and a chemotherapeutic agent. However, the Examiner asserts that such an effect was not unexpected because "IDO inhibitors were known to have chemosensitizing activity" (page 6 of the instant Official Action). The Examiner cites Sabol et al. (Biologica, Bratislava (2000) 55:701-707) in support of this assertion. Applicants respectfully disagree with the Examiner's position. Indeed, Sabol et al. clearly teach that the IDO inhibitor brassinin does **not** possess chemosensitizing activity.

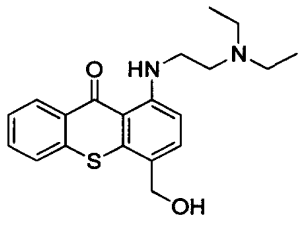
At the outset, Sabol et al. do not disclose IDO inhibitors in general. Rather, Sabol et al. is solely concerned with the cytotoxic effects of cruciferous phytoalexins. One of the compounds (brassinin) tested by Sabol et al., however, is identified in the instant application as an IDO inhibitor. The ability of brassinin to inhibit IDO is not taught by Sabol et al. Indeed, Sabol et al. state that the "mechanism of antineoplatic effect of brassinin is not known yet" (page 706). Accordingly, the prior art does **not** in any way teach or suggest that IDO inhibitor *in general* are chemosensitizers.

In support of the position that IDO inhibitors were known

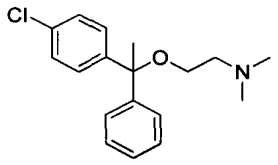
to have chemosensitizing activity, the Examiner has cited page 702 of Sabol et al. Specifically, Sabol et al. state that brassinin "could be considered as a candidate of chemosensitizing agents." Accordingly, Sabol et al. only initially hypothesized that brassinin ***could be considered a possible*** chemosensitizing agent. Sabol et al. subsequently show that brassinin is **not** a chemosensitizing agent in their assays. Indeed, at page 701, Sabol et al. clearly state that "**no** sensitizing effect of brassinin to vincristine cytotoxicity against resistant L1210/VCR line was found" (emphasis added). Figure 5 of Sabol et al. clearly shows that brassinin completely failed to enhance the cytotoxicity of vincristine at any concentration. In complete contrast, Sabol et al. demonstrate that verpamil, a "well-known chemosensitizer" (page 704), which is not identified as an IDO inhibitor, "sensitizes L1210/VCR cells to vincristine toxicity and reduces the growth of cells by 70%" (see Figure 5 and pages 704-705).

In view of the foregoing, it is evident that Sabol et al. 1) do not teach IDO inhibitors in general; 2) test the chemosensitizing ability of one compound (brassinin), which is identified by the instant application as an IDO inhibitor; and 3) definitely state that brassinin, the lone IDO inhibitor tested, does *not* chemosensitize the cancer cell lines tested.

It is also noteworthy that Sabol et al. rely on Efferth (Anticancer Res. (1991) 11:1275-9; Abstract provided) to make the statement that "brassinin due to aromatic and nitrogen components, could be considered as a candidate of chemosensitizing agents." Efferth et al., however, merely identify hycanthone and chlorophenoxamine as chemosensitizers.

The structure of hycanthone is 

and the

structure of chlorophenoxamine is  . Clearly, these compounds bear little to no structural resemblance to brassinin or the IDO inhibitors of the instant invention.

Inasmuch as IDO inhibitors were **not** known to have chemosensitizing activity prior to the instant application as alleged by the Examiner, the demonstration in the instant application of a greater than additive effect (see, e.g., the July 2, 2009 Official Action response) with the administration of an IDO inhibitor and a chemotherapeutic agent must be considered unexpected. Indeed, the prior art reference relied on by the Examiner clearly states that brassinin does not function as a chemosensitizer.

Lastly, claim 42 states that the IDO inhibitor is 1-methyl-tryptophan, claim 53 states that the IDO inhibitor is methyl-TH-DL-trp, and claim 54 states that the IDO inhibitor is 1-methyl-DL-trptophan. Applicants respectfully submit that the Examiner has clearly failed to provide a *prima facie* case of obviousness against these claims. Indeed, the Examiner has relied on a reference (Sabol et al.) which describes brassinin and the Examiner attempts to extrapolate this teaching to all IDO inhibitors. However, brassinin was not known as an IDO inhibitor prior to the instant application. Accordingly, even if brassinin was described as a chemosensitizer by Sabol et al. (which it is **not** for the reasons set forth above), then a skilled artisan still could not make the connection to IDO inhibitors in general because the instant application is the first description of the IDO inhibiting properties of brassinin. Accordingly, prior to the instant invention, there would be no nexus between brassinin and other IDO inhibitors, such as 1-methyl-tryptophan, methyl-TH-DL-trp, and 1-methyl-DL-trptophan. For the foregoing reasons, it is evident that the Examiner has failed to set forth a *prima facie* case of obviousness.

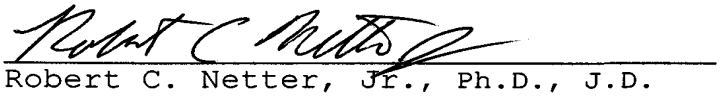
In view of the foregoing, Applicants respectfully submit that the rejection of claims 38, 39, 41-47, and 54-56 under 35 U.S.C. §103(a) is untenable and should be withdrawn.

CONCLUSION

In view of the foregoing remarks, it is respectfully urged that the rejections set forth in the December 31, 2009 Official Action be withdrawn and that this application be passed to issue.

In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to call the undersigned at the phone number given below.

Respectfully submitted,
DANN, DORFMAN, HERRELL AND SKILLMAN
A Professional Corporation

By 
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Enclosures: Efferth et al., Anticancer Res. (1991) 11:1275-9
(Abstract only)
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